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VIEWPOINTS

Drug-Eluting Stenting

The Case for Post-Dilation

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In clinical practice, adequate stent deployment has an important effect on immediate and long-term results after percutaneous coronary interventions. In particular, suboptimal or incomplete stent expansion is associated with increased restenosis and target vessel revascularization rates and, especially with drug-eluting stents (DES), might also predispose to stent thrombosis. Notwithstanding the significant improvement in technique and materials in the last decade, adjunctive high-pressure balloon dilation is still necessary to improve the minimum stent area and the uniform volumetric stent expansion in a majority of the cases. Indeed, in the published reports, the incidence of incomplete stent deployment ranges from 20% to 30% of cases, but it is significantly higher in trials in which stent expansion was assessed by intravascular ultrasound. Although there are not enough randomized studies about this topic, data from published reports continue to support the use of proper post-dilation in the majority of patients undergoing both bare-metal stent and DES implantation. This review will summarize the different anatomical, clinical, and device-related variables for increased risk of suboptimal stent delivery, highlighting the importance of adequate high-pressure post-dilation to obtain optimal stent expansion to positively affect stent thrombosis and restenosis. (J Am Coll Cardiol Intv 2008;1:22–31)

Optimization of stent deployment during percutaneous coronary intervention (PCI) is a key element to obtain most favorable immediate and long-term results. Since the introduction of balloon-expandable bare-metal stents (BMS) in common practice, the need was recognized for adequate stent expansion to avoid suboptimal stent deployment and reduce the incidence of target vessel revascularization (TVR) (1,2).

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Early-generation stents were delivered with a compliant balloon and systematically required further post-dilation with a noncompliant balloon at higher pressures to obtain an adequate lumen dilation and complete apposition of stent struts to the vessel wall (3–6). Notwithstanding the successive introduction of stent delivery systems based on a semi-compliant balloon allowing stent deployment at higher pressures (≥14 atm), post-dilation with a noncompliant balloon or using a larger balloon is still demanded to attain the principle "media to media" stent expansion (7–12).

After the introduction of drug-eluting stents (DES) that dramatically improved restenosis and TVR, the importance of optimal stent deployment was initially underestimated, leading to less use of balloon post-dilation. In the major randomized clinical trials (RCTs) testing DES, post-dilation was not routinely performed (13–15). Nevertheless, despite the lack of evidence from RCTs, observational data continue to support the use of adjunctive balloon post-dilation after deployment of DES in the great majority of patients (16–21). Indeed, the current stent delivery systems of DES are similar to if not the same as in BMS, and the risk of suboptimal stent

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expansion is still high. Importantly, suboptimal or incomplete stent expansion, especially with DES with polymeric coating, not only might be associated with increased restenosis and TVR, but also might predispose to stent thrombosis (21–25).

The aim of this paper is to review all the possible causes and consequences of a suboptimal stent expansion and assess the possible role of adequate high-pressure balloon post-dilation to prevent it in the DES era.

Diagnosis and Magnitude of Suboptimal Stent Deployment: Role of Intravascular Ultrasound (IVUS)

Because stent underexpansion is poorly recognized by angiography, the real incidence of suboptimal stent deployment is likely to be underestimated. Indeed, it has been observed that discrepancies exist between angiographically-defined and IVUS-defined optimal stent deployment regardless of the stent implanted, with the IVUS success rate raging from 13% to 70% despite successful angiographic results (1,18,26–28). A comparison example between angiographic and IVUS results before and after high-pressure stent post-dilation is shown in Figure 1.

An IVUS analysis is more accurate than angiography in determining in-stent dimension and is able to better detect subtle findings such as incomplete apposition and dissection at the stent edges (29–33). Several trials in which stent expansion was assessed by IVUS, such as the STRUT (Stent Treatment Region assessed by Ultrasound Tomography) (34), CRUISE (Can Routine Ultrasound Influence Stent Expansion) (7), and AVID (Angiography Versus Intravascular Ultrasound Directed Coronary Stent Placement) (35) studies, showed an incidence of post-procedural incomplete BMS deployment raging from 4% to 22% (36). Similarly, a high rate of inadequate expansion, ranging between 24% and 28%, has also been observed with current DES (18).

Moreover, IVUS measurements have provided powerful predictive information regarding stent thrombosis, restenosis, and TVR. In particular, minimal stent area (MSA) and minimal stent diameter (MSD) measured by IVUS at the end of the procedure are the strongest predictors of TVR after BMS implantation in numerous studies (37–41). Therefore, IVUS should be considered the gold standard to verify the final result of a PCI procedure and should be recommended in those situations with increased risk of suboptimal stent deployment. Unfortunately this statement, even if it seems reasonable, is so far supported only by "personal opinion" (Level of Evidence C).

One of the main problems in this field is the lack of a uniform and accepted definition of optimal stent expansion by IVUS. Whereas angiographic optimal stent expansion can be qualified as 0% residual stenosis, such a clear definition is not present in the IVUS published data.

The first study that prospectively evaluated the effect of optimal stent expansion according to specific IVUS definitions was the MUSIC (Multicenter Ultrasound Stenting in Coronaries) study (2). Table 1 shows the IVUS criteria introduced in the MUSIC study to define "optimal" stent expansion. Subsequently, other studies assessing the role of IVUS-guided stent delivery adopted slightly different criteria, which are summarized in Table 2.

In our view, the main limitation present in all criteria proposed is that none of them takes the advantage given by positive remodeling at the lesion site. The presence of positive remodeling at the lesion site allows the dilation of the stent to a size larger than the distal lumen. This advantage is particularly important when using long stents, where it is useful to size each segment as close as possible to the real dimensions of the vessel and not just to an extrapolated target taken from 2 references (proximal and distal) that are very far from each other. In such circumstances, criteria using an average between the lumen proximal and distal to the stent, such as in the TULIP (Thrombocyte activity evaluation and effects of Ultrasound guidance in Long Intracoronary stent Placement) study (8), becomes of limited value, owing to the discrepancies between proximal and distal lumen sizes. The closer we are to the proximal or distal end of a long stent, the larger will be the inappropriate value of this target criterion.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CSA = cross-sectional area
DES = drug-eluting stent(s)
IVUS = intravascular ultrasound
MSA = minimal stent area
MSD = minimal stent diameter
PCI = percutaneous coronary intervention
RCT = randomized clinical trial
SES = sirolimus-eluting stent(s)
TVR = target vessel revascularization

The recently launched AVIO (Angiography Versus IVUS Optimisation) study, which has been designed to compare the long-term results with DES with an IVUS-guided strategy versus an angiographic strategy, will use a novel criteria (i.e., a minimal luminal area ≥70% the nominal balloon cross-sectional area [CSA] used to dilate a specific segment of the stent) to define optimal stent implantation. In addition, in this study, post-dilation non-compliant balloon size will be selected according to the average (maximum and minimum diameter) of the media to media diameter at the following points: distal in-stent segment, proximal in-stent segment, and point in-stent of maximal narrowing. Alternatively a lumen CSA >9 mm^2 will be considered adequate. In our opinion, these new definitions will overcome the limitations used in previous IVUS-guided RCTs.

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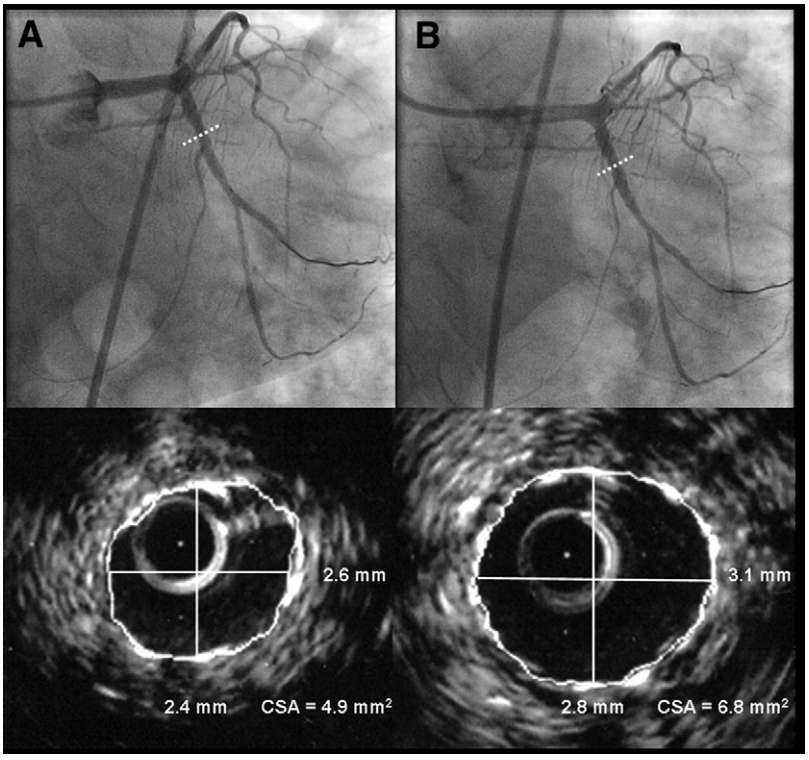

Figure 1. Comparison of Angiographic and IVUS Findings Before and After High-Pressure Stent Post-Dilation

Comparison of angiographic and intravascular ultrasound (IVUS) results after high-pressure stent deployment **(A)** and after post-dilation with a noncompliant balloon of the same size **(B)**. Note that by angiography, no clear difference can be seen before and after the post-dilation. Conversely IVUS demonstrates a significant increase in lumen cross-sectional area (CSA) after a noncompliant balloon post-dilation.

Determinants of Suboptimal Stent Deployment

Stent undersizing. Among the possible reasons for suboptimal stent deployment, the first is certainly the undersizing of the stent delivery balloon related to the target vessel.

Table 1. Optimal Stent Expansion Criteria Adopted in the MUSIC Study

IVUS Criteria Defining Optimal Stent Deployment	
1	Complete apposition of the stent over its entire length against the vessel wall.
2A	In case the in-stent luminal area <9.0 mm²: • In-stent minimal lumen area ≥90% of the average reference lumen area or ≥100% of lumen area of the reference segment with the lowest lumen area; • In-stent lumen area of proximal stent entrance ≥90% of proximal reference lumen area.
2B	In case the in-stent luminal area >9.0 mm²: • In-stent minimal lumen area ≥80% of the average reference lumen area or ≥90% of lumen area of the reference segment with the lowest lumen area; • In-stent lumen area of proximal stent entrance ≥90% of proximal reference lumen area.
3	Symmetric stent expansion defined by LDmin/LDmax ≥0.7.

IVUS = intravascular ultrasound; LDmax = maximum lumen diameter; LDmin = minimum lumen diameter; MUSIC = Multicenter Ultrasound Stenting in Coronaries.

Indeed, in patients with severe and diffuse target vessel disease, the choice of the correct stent size on the basis of only angiographic evaluation is often difficult and leads very often to a balloon to artery ratio <1 (42,43). Our group clearly demonstrated that assessment of the reference vessel diameter in coronary arteries significantly varies according to the method of measurement used; a difference between IVUS and angiography >1.0 mm was found in 71% of cases with vessel size <2.75 mm and in 49% of cases in patients with vessel size >2.75 mm, respectively (42).

Similarly, the recent practice of direct stenting might increase the risk of stent undersizing, especially when handled by nonexperienced operators and when used to treat severe stenotic lesions preventing the correct estimation of the distal vessel size.

It is worth noting that in case of undersizing of the stent delivery balloon, high-pressure stent deployment, especially with the current semi-compliant balloon, can compensate for the balloon undersizing only in part.

Balloon device compliance and pressure deployment. Another possible cause of stent underexpansion is strictly related to the compliance of balloons commonly used in delivery systems that are often not adequate to guarantee full

Table 2. Optimal Stent Expansion Criteria Adopted in the Studies Assessing the Role of IVUS-Guided Post-Dilation

Study (Ref. #)	Study Design	Primary End Point	Effect of IVUS-Guided Post-Dilation on Primary End Point	Ultrasound Criteria of Optimal Stent Expansion	Rate of Patients Fulfilling IVUS Criteria After Post-Dilation
Albiero et al. (4)	Case-control study	Dichotomous angiographic restenosis (>50% stenosis)	NS	1) Achievement of complete stent apposition to the vessel wall; 2) Stent lumen CSA ≥ the distal reference lumen CSA; 3) Absence of significant lesion in nonstented adjacent inflow and outflow segments	Not available
RESIST (68)	Multicenter randomized	6-month angiographic restenosis (>50% stenosis)	NS	1) Intrastent CSA ≥80% of the average of the proximal and distal reference lumen CSA	80%
AVID (35)	Multicenter randomized	Cumulative rate of death, MI, or coronary artery bypass graft surgery	NS	1) MSA ≥90% of average reference lumen area by IVUS; 2) Absence of dissection; 3) Complete stent apposition	57%
CRUISE (7)	Case-control study	Post-procedural MLD by QCA and IVUS	Positive	Left to operator's choice	NA
SIPS (70)	Multicenter randomized	6-month angiographic MLD	NS	1) Complete stent apposition; 2) In-stent minimal lumen area ≥90% of the average reference lumen area or ≥100% of lumen area of the reference segment with the lowest lumen area; 3) Symmetric stent expansion defined by LDmin/LDmax ≥0.7	50%
OPTICUS (69)	Multicenter randomized	6-month angiographic restenosis (<50% DS), MLD, and %DS	NS	1) Complete stent apposition; 2) In-stent minimal lumen area ≥90% of the average reference lumen area or ≥100% of lumen area of the reference segment with the lowest lumen area; 3) Symmetric stent expansion defined by LDmin/LDmax ≥0.7	56%
TULIP (8)	Multicenter randomized	6-month MLD and MACE (death/MI/TLR)	Positive	1) Complete stent apposition; 2) In-stent MLD >80% of the mean of average vessel reference diameter; 3) In-stent MLA greater than or equal to distal reference lumen area	89%
PRESTO IVUS substudy (71)	Multicenter randomized	9-month MACE (death/MI/ischemia-driven TVR)	NS	Left to operator's choice	NA

AVID = Angiography Versus Intravascular ultrasound Direct stent implantation; CRUISE = Can Routine Ultrasound Influence Stent Expansion; CSA = cross-sectional area; DS = diameter stenosis; MACE = major adverse cardiac events; MI = myocardial infarction; MLA = minimal lumen area; MLD = minimal lumen diameter; MSA = minimal stent area; NA = not applicable; NS = not significant; OPTICUS = Optimization with ICUS to reduce stent restenosis; PRESTO = Prevention of Restenosis with Tranilast and its Outcomes; QCA = quantitative coronary angiography; RESIST = Restenosis after IVUS-guided Stenting; SIPS = Strategy for Intracoronary ultrasound-guided PTCA and Stenting; TLR = target lesion revascularization; TULIP = Thrombocyte activity evaluation and effects of Ultrasound guidance in Long Intracoronary stent Placement; TVR = target vessel revascularization; other abbreviations as in Table 1.

stent expansion at nominal pressures (26). Stent manufacturers provide a compliance chart relating balloon deployment pressure and the stent diameter. Nevertheless, compliance charts are based on in vitro measurement (in air or in water), exclusively depending on material properties or design features of the stents themselves (44), but in vivo stent expansion is mainly limited by lesion and vessel compliance. Several IVUS studies found that the real MSD after stent deployment was 20% to 26% less than the unconstrained stent size displayed in the compliance chart on the stent box (9,10,18,20,26,45). These differences were independent of stent manufacturer, length, diameter, and deployment pressure and related to the inherent resistance of dilating a stent within an atherosclerotic artery (26,28).

Notwithstanding these discrepancies, the manufacturers' compliance charts are routinely used by interventional cardiologists to optimize stent diameter according to inflation pressure during PCI. Thus, in clinical practice, the pressure level at which the stent is deployed probably represents the critical determinant of final stent expansion and apposition to the vessel wall. The importance of this issue has not changed with the new stent delivery systems based on semi-compliant balloons, and DES showed the same properties as the corresponding BMS platforms (46). Therefore, high-pressure stent deployment is still strongly recommended to obtain full expansion of both BMS and DES. In this context, IVUS analysis might have a role to check whether the pressures used have really fulfilled the job to optimally deploy the stent.

Plaque and vessel compliance. In IVUS studies, arterial expansion seemed to be the primary mechanism of lumen enlargement after stenting, accounting for approximately 70% of luminal gain, whereas the relative contribution of plaque reduction ranged between 6% and 34% (47–49). Therefore, the presence of calcium or fibrosis that impairs distensibility of the vessel wall and the presence of high plaque burden behind the stent might represent major limitations to complete stent opening (50).

In this context, the negative influence of plaque burden on adequacy of deployment has been demonstrated by Yoon et al. (28) in a single center study on consecutive patients undergoing stent implantation with IVUS examination. Nevertheless, in this study, the effect of stent post-dilation has not been assessed. Similarly, calcified vessels affect final stent lumen area, preventing complete expansion even when higher pressures or larger balloons are applied (51). In this situation, the use of high-pressure balloon inflations determines vessel overexpansion at noncalcified segments rather than compression of the calcific plaque. The net result is that a significant portion of stent remains underexpanded and asymmetric, which in turn probably explains the higher rate of restenosis found in this type of lesion (39,52).

Therefore, in these situations, when ablative or atherectomy techniques are not feasible, the use of a noncompliant balloon post-dilation represents a good compromise to achieve good stent expansion and symmetry without increasing risk of dissection or rupture of the vessel. In studies in which IVUS analysis after post-dilation was accomplished, including the POSTIT (Postdilatation Clinical Comparative Study) trial (10), none of the baseline clinical or angiographic variables seemed able to predict the final MSA or MSD after stenting. Similarly, neither quantitative IVUS lesion measurements nor qualitative IVUS assessment of plaque morphology could predict stent expansion (18). These observations would suggest that the impact of plaque and vessel compliance on the final stent expansion can be limited by an appropriate use of post-dilation.

Lesion characteristics. Specific lesion subsets are associated with a lower success rate and required more care and tools to obtain an optimal stent deployment. Lesion subsets in which adequate post-dilation should be carefully considered are summarized in Table 3.

BIFURCATION LESIONS. Bifurcation treatment is associated with a high incidence of nonuniform stent expansion in the side branch, resulting in a higher TVR rate (53). Indeed, the lateral opening of the stent in the main branch to gain access to the side branch causes strut deformation and malapposition (54–57). In this context, several studies showed that in bifurcation lesions, especially in the case of both branches stenting, final post-dilation with a kissing balloon is associated with more favorable long-term outcome, reducing the restenosis rate of the side branch and the need for TLR (57–59). Thus, kissing balloon dilation at the end of the procedure is mandatory for bifurcations, but balloon diameters and inflation pressures are yet to be defined to uniformly expand stent struts in both branches. In this context, the use of adequately sized noncompliant balloons at truly high pressures might represent a good compromise between safety and efficacy.

Table 3. List of Conditions Associated With an Increased Risk of Suboptimal Stent Deployment

Low-pressure stent deployment (<12 atm)
Lesions with heavy calcification
Lesions with large plaque burden (severe stenosis)
Lesions with a mismatch of proximal and distal reference size
Ostial lesions
Bifurcation lesions treated with stenting of side branch
Long lesions requiring multiple stent
Small vessel treatment
Treatment of diffuse in-stent restenosis

LONG LESIONS. Although lesion length does not influence stent expansion per se (44), the RENEWAL (Randomised Trial of Endoluminal Reconstruction Comparing the NIR Stent and Wallstent in Angioplasty of Long Segment Coronary Disease) and MUSIC trials showed that the high restenosis rates with long stents might be related to a suboptimal stent deployment (2,60). Treatment of long lesions, especially when more than 1 stent is required or when long stents are implanted, increases the risk of size mismatch between the proximal and distal portion of the target vessel. Indeed, in such cases, the stent is usually sized for distal reference diameter and results undersized for the proximal reference diameter. Furthermore, the presence of a double stent struts layer could reduce vessel compliance and can produce an incomplete stent apposition beneath the overlap. For these reasons, a systematic post-dilation of the proximal portion of a long stent and of the overlapping zone with high-pressure inflations or a larger balloon is strongly recommended.

SMALL VESSELS. In clinical practice, many interventional cardiologists generally avoid implantation of stents with a diameter size smaller than 2.5 mm. Thus, for small vessels it is common practice to deploy stents that are slightly larger but at lower pressures to avoid excessive vessel overstretch. This habit results in very high incidence of suboptimal stent deployment and an increased incidence of TVR (20). As previously described, in this context it is fundamental to assess whether the vessel is really a small vessel or just appears as such at angiography. Nitroglycerine administration, IVUS evaluation, and bearing in mind that the left anterior descending artery is rarely a small vessel unless in its distal segment are important concepts. If the vessel's small size were confirmed, post-dilation at higher pressures with a 2.5-mm noncompliant balloon would represent an indispensable solution to achieve the largest final lumen stent to reduce the risk of stent thrombosis and TVR.

IN-STENT RESTENOSIS. Although DES use has also provided encouraging results in this setting, stent underexpansion is the main predictor of in-stent restenosis, ranging between 20% and 40% of the cases (61–66). Interestingly, Blackman et al. (67) showed that a noncompliant balloon post-dilation is necessary during treatment of in-stent restenosis to achieve luminal gain through further expansion of the original stent, which cannot be obtained with a second stent deployment alone. In this study, after post-dilation with a

noncompliant balloon, the number of patients with optimal stent expansion according to the IVUS criteria increased from 33% to 67%. Thus, this study also demonstrated that, with post-dilation with noncompliant balloons, significant stent re-expansion can be obtained during repeat angioplasty irrespective of the grade of initial stent underexpansion.

High-Pressure Stent Deployment Versus Noncompliant Balloon Post-Dilation

Several studies (3,6) demonstrated that supranominal pressures are frequently not enough to offset the high impedance of diseased artery. In particular Bermejo et al. (6) showed that, despite high-pressure stent deployment, only 55% of achievable acute lumen gain was effectively obtained, suggesting that plaque characteristics and vessel resistance often cause inadequate expansion of semi-compliant balloons. Unfortunately, there is no guarantee that simple high-pressure post-dilation with a noncompliant balloon will result in final optimal stent deployment.

Consequently, in the subsequent years, the use of IVUS to optimize stent implantation became common practice, and several studies evaluated its role in PCI outcome. The MUSIC study was the first large study that assessed the role of IVUS-guided post-dilation to optimize stent deployment, demonstrating its favorable impact on immediate and 6-month clinical and angiographic results (2).

Similarly, the POSTIT (10), CRUISE (7), and TULIP (8) studies clearly showed that systematic IVUS-guided post-dilation can provide a larger minimal stent area and how this might translate into better long-term outcome. In particular, the multicenter POSTIT trial (10) showed that adjunctive a noncompliant balloon post-dilation can double the frequency of achieving optimal stent deployment when compared with high delivery pressures. Furthermore, the CRUISE study demonstrated the clinical relevance of this approach, showing that an increase of 14% of the final MSA obtained in the IVUS-guided group resulted in a 44% composite relative reduction in TVR (7).

In contrast, other contemporary studies, such as the RESIST (REStenosis after IVUS-guided STenting) (68), OPTICUS (Optimization with ICUS To Reduce Stent Restenosis) (69), SIPS (Strategy for Intracoronary ultrasound-guided PTCA and Stenting) (70), and PRESTO (Prevention of Restenosis with Tranilast and its Outcomes) (71) studies, did not confirm the benefit derived from IVUS guidance for post-dilation on long-term results.

Although there is a trend toward a benefit in TLR favoring IVUS-guided coronary stent implantation, especially in high-risk lesion subtypes (e.g., saphenous vein grafts, long lesions), the effect on long-term death and nonfatal myocardial infarction is neutral (72).

The choice of more conservative IVUS criteria and the consequent less aggressive stent post-dilation (Table 2), the heterogeneity with respect to the rate of patients fulfilling the pre-specified IVUS criteria at the end of procedure, and the underpowered design in most negative studies constitutes possible explanation of these conflicting results. Nevertheless, apart from their specific characteristics and results, all of the studies cited in the preceding text undoubtedly demonstrated that an adequate post-dilation is required to assure an optimal stent deployment in most of the lesions, independently from the original pressure of stent deployment.

Compliant Versus Noncompliant Balloon Post-Dilation

For safety and deliverability reasons, most of the stent delivery systems are currently based on a semi-compliant balloon device. The compliant nature of these balloons causes significant deformation of profile and volume with increases in pressures, resulting in stretching of the balloon itself. Thus, although current semi-compliant balloons are precisely matched with stent length with very short balloon shoulders and assure a uniform diameter expansion along the balloon length, the risk of vessel stretch and edges injury is important at high pressures. Similarly, this technical aspect must be carefully considered during high-pressure stent post-dilation with semi-compliant balloons.

Conversely, noncompliant balloons have little change in volume, even at high pressures concentrating dilating force at the lesion site (73). Indeed, bench tests and clinical studies have shown that noncompliant balloons exert more dilating force against a lesion or a stent than compliant balloons for a given balloon size and inflation pressure. Thus, post-dilation with noncompliant balloons actually results in a significant improvement of MSA compared with the current semi-compliant stent deployment balloons. Especially, the use of a noncompliant balloon post-dilation avoids using a balloon larger than the reference vessel and also allows the application of very high pressures (just below the rated burst pressure) in a safe manner. The main difference between compliant and noncompliant balloons during high-pressure inflation is shown in Figure 2.

These features can be important to prevent unwanted and potentially severe complications caused by over-dilation or uncontrolled fast stretch of the vessel wall. Using a compliant balloon at high pressures, for example, in calcified or very stiff lesions might cause dissection at stent edges and, in small vessels, might facilitate coronary rupture. Several animal and human studies suggested that aggressive stent inflation with high pressures, causing deeper injury of the vessel wall with rupture of the intima or media (74–76), might result in a long-term inflammatory response with a greater neointimal proliferative response and an increased restenosis rate (77,78). Moreover, a SIRIUS (SIRolImUS-Eluting Stent in De Novo Native Coronary Lesions) IVUS substudy (79) suggested that more injury to the contiguous

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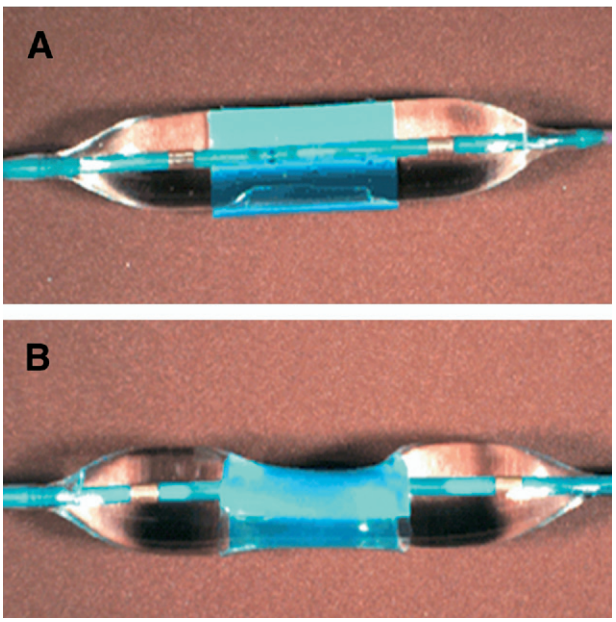

Figure 2. Difference Between Compliant and Noncompliant Balloons During High-Pressure Inflation

Bench test showing the different profile between a noncompliant balloon **(A)** and a semi-compliant stent delivery balloon **(B)** during high-pressure (>14 atm) inflation. The semi-compliant balloon demonstrates a "dog bone" effect at the edge of the cylinder that can damage the vessel wall in vivo.

vasoelastic normal wall, coupled with a drug that delays the healing process, could contribute to late stent malapposition owing to focal positive vessel remodeling.

These considerations should lead to more common use of a noncompliant balloon for post-dilation at high pressure.

Benefits of a Noncompliant Balloon Post-Dilation After DES Implantation

The main consequences of stent underexpansion are represented by higher rate of restenosis and related necessity of repeated revascularization at long-term follow-up. Moreover, with DES, potential increase in the risk of stent thrombosis exists (80,81).

In-stent restenosis. Several studies demonstrated the importance of complete strut apposition, luminal CSA, and concentricity of the stent implanted (29,82). According to these data, IVUS measurement of MSA is the single most powerful predictor of long-term patency and clinical outcome with an inverse relation between post-procedural MSA and angiographic restenosis and between MSA and TVR (4,37,38,40,83). In the TULIP study (8), for example, restenosis rate was 23% in the group guided by IVUS versus 45% in the angiography group, whereas the CRUISE trial (7) demonstrated a relative TVR reduction of 44% when stent underexpansion was corrected by IVUS.

With the advent of DES, determining a lower rate of angiographic restenosis and clinical TVR, the need for adjunctive balloon post-dilation was considered less important. Moreover, the possible role of vessel trauma at the stent margins owing to pre- and post-dilation in determining sirolimus-eluting stent (SES) edge restenosis in the SIRIUS trial (14) led to a more extensive use of direct stenting, whereas post-dilation was used only if strictly required by suboptimal angiographic stent placement (84). In particular, a comparison study (85) between SIRIUS-US (pre- and post-dilation) and E-SIRIUS (direct stenting and nonmandatory post-dilation) IVUS results showed that, although the less aggressive stent implantation in E-SIRIUS resulted in a relatively lower stent expansion, no detrimental effects were observed in major adverse cardiac events.

Subsequently, serial IVUS analyses from the SIRIUS trial showed that, whereas a smaller MSA might be acceptable after DES, underexpansion can result in restenosis (21). This finding was confirmed in other studies in which an incidence of 60% to 70% stent underexpansion determining an MSA <5.0 mm^2 was found in most of the cases of SES failures (86–88). Moreover, specific IVUS analysis of DES failure demonstrated a correlation between non-uniform stent strut distribution and maximal neointimal hyperplasia, suggesting local drug underdosing as mainly responsible for this phenomenon (16,89).

In conclusion, observational data suggest that stent underexpansion might be one of the most important causes of DES failure, advocating that, once neointimal hyperplasia is suppressed, the optimum stent deployment is still fundamental. Therefore, post-dilation with noncompliant balloons at high pressures, improving final MSA and MSD, might greatly increase the frequency of optimum DES deployment and actually lead to reduction of restenosis and TVR rates. To specifically address the exact role of high-pressure noncompliant post-dilation strategy, randomized clinical studies are warranted in the DES era.

Stent thrombosis. Stent thrombosis remains a potential devastating complication in patients undergoing PCI. In the current era of high-pressure stent implantation, the occurrence of stent thrombosis with BMS ranges from 1% to 2% (36,90). Conversely, the rate of DES thrombosis ranges between 0.4% to 0.6% (14,15) of the randomized trials and 1.3% to 4.9% of "real world" registries (24,80).

The major post-procedural predictors of thrombosis with both BMS and DES are MSA and suboptimal stent expansion (23,36,91); in particular, stent underexpansion, resulting in abnormal shear stress, might explain as much as 80% of those events (22,92).

In a large registry of 7,484 consecutive patients treated with BMS, only 22% of patients that experienced subacute

stent thrombosis had an optimum PCI result as assessed by IVUS. In this study, the IVUS analyses of thrombosed stents revealed an inadequate lumen dilation (final lumen <80% reference lumen) in 78% of cases, edge dissection in 17%, malapposition in 9%, and plaque prolapse in 4% (92).

The importance of complete stent expansion to prevent stent thrombosis might be more relevant with DES. Indeed, decreased endothelialization associated with drug-related inhibition of neointimal proliferation might increase the risk of stent thrombosis in the case of suboptimal stent expansion. Fujii et al. (23) showed in a retrospective study that lesions leading to stent thrombosis after successful SES implantation more often have stent underexpansion, smaller MSA, and residual edge stenosis. This evidence has also been confirmed for the late-thrombosis cases of DES (>12 months) (91), but in this case, the pathophysiology mechanism is likely more complex (e.g., late acquired incomplete stent apposition) and not completely understood (93).

In this view, the less care used by operators to obtain an optimal stent deployment and a lower use of post-dilation might represent a possible explanation of the higher rates of stent thrombosis observed with DES. Thus, in absence of conclusive data regarding DES long-term safety, it is reasonable to hypothesize that a return to the "antique" practice of a noncompliant balloon post-dilation could also result in an overall reduction of the risk of stent thrombosis with DES.

Conclusions

In clinical practice, according to the rate of suboptimal stent deployment reported in different studies, a considerable number of patients might benefit from repeat inflations with noncompliant balloons at higher pressures and/or with larger diameter size. Indeed, although incomplete stent expansion was attributed as a defect of the first-generation balloon-expandable stent, several studies demonstrated that adjunctive balloon dilation is still necessary to improve the minimum stent area and the volumetric expansion throughout the stented segment.

Data from the literature suggest that achieving adequate stent expansion during PCI is important to reduce restenosis and the need for TVR, but it might also minimize the risk of stent thrombosis in the DES era. Although there are not enough randomized data to support its use, it seems wise to perform post-dilation with noncompliant balloons at high pressures in the majority of patients undergoing both BMS and DES implantation. Particularly in IVUS-guided procedures, the recommended strategy to achieve an optimal stent deployment should be to select a noncompliant balloon whose size matches the media-to-media IVUS measurement.

Unfortunately, it is not practical and cost-effective to perform post-dilation in all patients undergoing stent implantation. A more reasonable approach would then be to select those situations in which the risk of suboptimal stent delivery is higher, especially when DES are employed.

Randomized controlled trials to assess the role of IVUS-guided optimal stent implantation with DES are warranted.

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